

### **REMARKS**

In this Amendment, Applicant has amended Claim 4 to specify different embodiments of the present invention and overcome the rejection. It is respectfully submitted that no new matter has been introduced by the amended claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

#### **REJECTIONS UNDER 35 U.S.C. § 112 FIRST PARAPGRAPH:**

Claims 4 – 6 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains to make and use the invention.

It is respectfully submitted that in view of the present amendments to the Claims 4 – 6, the rejection has been overcome. More specifically, Claim 4 has been amended to define the specific biological activity to influence viscoelastic properties of hepatocyte membranes and the term “and lower” has been deleted. Applicant respectfully submits that the currently claimed subject matter is described in the specification in the way that enables one skilled in the art to make and use the invention. For instance, Example 5 of the specification shows the procedure of determining the effect of the glycoprotein on viscoelastic properties of hepatocyte membranes. The essence of the experiment consists in the following procedures: Kidney fragments were cultured with a glycoprotein solution. At the same time, a comparative experiment for control is conducted in which there is no addition of glycoprotein solution during culturing. Thenm these kidney fragments are subject to destructive attack as a result of which partial hepatocyte membrane destruction occurs releasing single cellular nuclei. The amount of the released cellular nuclei is directly dependent on viscoelastic properties of the hepatocyte membrane, i.e., the stronger and more elastic a membrane is, the less hepatocytes are destructed, the less cellular nuclei are released. The effect of glycoproteins on

viscoelastic properties of the hepatocyte membrane may be both positive and negative. In addition, the effect may be different at various glycoprotein concentrations, for example, positive at one concentration and negative at another concentration. It is important to point out that all the claimed glycoprotein affect viscoelastic properties of the hepatocyte membrane as defined and in the claimed super low doses. This is sufficiently supported by the original disclosure of the present invention.

Regarding the pharmaceutical efficacy of glycoprotein, a number of examples have been provided by the original specification. For instance, Example 6 studies the effect of the main thymus glycoprotein on hypersensitivity reaction of delayed-type. The therapeutic effect of Basic thymus glycoprotein (BTG) is shown in the dose of  $2 \times 10^{-12}$  g per animal to stimulate hypersensitivity reaction of delayed-type caused by the function of type 1 helper T-lymphocytes, which influence development of specific anti-tumor immunity reactions. Similarly, Example 8 of the original specification studied the effect of thymus acid glycoprotein on hypersensitivity reaction of delayed-type. In addition, Example 7 of the original specification disclosed the effect of main thymus glycoprotein on the survival of mice having EL4 thymoma. It is shown in the data that the glycoprotein in the dose of  $2 \times 10^{-12}$  g per mouse results in a statistically reliable increase in longevity of experimental animals – a group that received a minimum dose of tumor cells ( $1 \times 10^3$ ). Example 13, as disclosed in the specification, studied the effect of acid glycoprotein from liver on permeability of hepatocyte plasmatic membrane and protein synthesis intensity *in vitro*. Results of this investigation show that AGP affects protein synthesis intensity in hepatocytes and permeability of their plasmatic membranes in a super-small dose provided that the liver tissue structure is maintained. Similarly, Example 14 of the specification studied the effect of glycoprotein from mammalian blood serum (pI in the pH region of 4.65 – 5.1) on permeability of hepatocyte plasmatic membrane and protein synthesis intensity *in vitro*. Besides the above examples showing the type of glycoprotein biological activity, which can be used to produce therapeutic effect when glycoprotein are utilized as a medicament, the specification includes Example 15 – 17 of pharmaceutical compositions, which may be used as a medicament. It is respectfully submitted that the medical preparation “Adgelon” (substance), “Adgelon eye drops” and “Adgelon solution for intra-articular injections” have been registered by

the Ministry of Health of The Russian Federation (copies enclosed). The "Adgelon eye drops" pharmaceutical preparation is permitted for use in ophthalmology. The main conditions treated by such preparation include keratopathy and cornea erosion, keratitis, including herpetic and adenoviral, eye burns, cornea penetrating wounds. The pharmaceutical preparation of "Adgelon solution for intra-articula injections" is permitted for the use in rheumatology. The main indications for use is for large articulation osteoarthritis. Presently, pre-clinical and clinical investigations are being carried out of a number of other pharmaceutical preparations created on the basis of glycoprotein described in the present invention. These pre-clinical investigations have proven that all of them possess a therapeutic effect in super-small doses. It is respectfully submitted that a person skilled in the art will be able to make and use the present invention as disclosed.

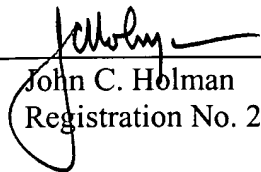
Therefore, the rejection under 35 U.S.C. § 112, first paragraph has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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By   
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Enclosure:

Copies of Registration Certificates of the medical preparations "Adgelon" (substance), "Adgelon eye drops" and "Adgelon solution for intra-articula injections" have been registered by the Ministry of Health of The Russian Federation